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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/090,672	06/04/98	ISHIWATA	T 766.21

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EXAMINER	
NIKODEM,D	
ART UNIT	**PAPER NUMBER**
1633	12

DATE MAILED: 05/24/00

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

File

Office Action Summary	Applicati n No.	Applicant(s)	
	09/090,672	ISHIWATA ET AL.	
	Examin r	Art Unit	
	David Nikodem	1633	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondenc address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).

Status

1)☐ Responsive to communication(s) filed on _____ .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-21* is/are pending in the application.

4a) Of the above claim(s) *3,6,8-17,20 and 21* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1, 2, 4, 5, 7, 18 and 19* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

13)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

a)☐ All b)☒ Some * c)☐ None of the CERTIFIED copies of the priority documents have been:

1.☒ received.

2.☐ received in Application No. (Series Code / Serial Number) _____ .

3.☐ received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. & 119(e).

Attachment(s)

15) ☒ Notice of References Cited (PTO-892)
16) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
17) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *4* .
18) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
19) ☐ Notice of Informal Patent Application (PTO-152)
20) ☐ Other: .

DETAILED ACTION

Claims election

1. Applicant's election of Group 1, claims 1-5,7,10-13,18 and 19 in Paper No. 8 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)). Claims 6, 8, 9, 14-17, 20 and 21 are withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to a non-elected invention.

2. It is noted that upon further review of this application, that claims 1-5,7,10-13,18 and 19 are drawn to nucleotides, nucleotide constructs, and/or nucleotide constructs that contain more than **ten** individual, independent and distinct nucleotide sequences in alternative form. Accordingly, these claims are subject to restriction under 35 USC 121 as outlined in 1192 O.G. 68 (Nov. 19, 1996).

3. Applicant is required to select no more than ten of the individual sequences for examination. The search of the no more than ten sequences may include the complements of the selected sequences and, where appropriate, may include subsequences with in the selected sequences (e.g., oligomeric probes and primers).

4. During a telephone conversation with Lawrence Perry on May 18, 2000 a provisional election was made with traverse to prosecute SEQ ID NO:1 to SEQ ID NO:6 and SEQ ID NO:9 to SEQ ID NO:12 of the invention previously elected. The

previously elected claims which correspond to the newly elected nucleotide sequences are claims 1, 2, 4, 7, 18 and 19. Affirmation of this election must be made by applicant in replying to this Office action. Claims 3 and 10-13 are withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to a non-elected sequences. Claims 1, 2, 4, 5, 7, 18 and 19 will be examined only to the extent that they read on the elected nucleotide sequences, namely, SEQ ID NO:1 to SEQ ID NO:6 and SEQ ID NO:9 to SEQ ID NO:12.

Claim Rejections - 35 USC § 101

5. 35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

6. Claims 1, 2, 4, 5, 7, 18 and 19 are rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter.

7. The claims as written are drawn to DNAs found in nature and do not show the hand of man. The language "a DNA" in the claims is interpreted broadly to read on DNA in a whole organism (*in vivo*). The claims as written read on any DNA from any organism. Claims directed to or including within its scope a human (e.g. a human with the cellular material) will not be considered patentable subject matter under 35 U.S.C. 101. The grant of a limited, but exclusive property right of a human being is prohibited by the Constitution. See 1077 OG 24. It is suggested that the language "isolated" be used to introduce DNA.

ok

Claim Rejections - 35 USC § 112

8. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter, which the applicant regards as his invention.

9. Claims 1, 2, 4, 5, 7, 18 and 19 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The language "related" and "represented" are vague and indefinite with regard to the definition of the terms "related" and "represented." By the language "related" it is unclear as to whether applicants intend to signify DNA that is increased in patients with IgA nephropathy, or whether DNA that is present only in patients with the disease, or whether DNA that is structurally related IgA DNA of the disease. Additionally, by the language "related" and "represented" it is unclear as to what specific nucleotide identity and/or homology to the SEQ ID Nos. is required for the claimed DNA. It is unclear whether the language is open or closed claim language and whether or not nucleotide flanking sequences and/or DNA allelic variants are embraced by the claims. The metes and bounds of this claim language are unclear. The claim language needs to describe distinctly and clearly the claimed invention(s). ok

10. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

11. Claims 1, 2, 4, 5, 7, 18 and 19 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

12. The use of the claim language "related," represented" and "under stringent conditions" allows for high variability as to the structure and/or identity of the claimed nucleotide sequence(s). The claims encompass a broad genus of nucleotide sequences, with the inclusion of allelic variants of the claimed DNAs and/or DNA with nucleotide flanking sequences. The specification fails to clearly define the structure and/or identity of the DNAs as described in the claims. The general knowledge in the art concerning DNA alleles does not provide any indication of how the structure of one allele is representative of other unknown alleles having concordant function. The nature of alleles is that they are variant structures where the structure and function of one does not provide guidance to the structure and function of others. Furthermore, DNAs with flanking sequences may or may not have hybridization properties similar to the parent DNA. In view of such, one of skill in the art would conclude that applicant was not in possession of the claimed invention as depicted by the claim language.

ok

13. Claims 1, 2, 4, 5, 7, 18 and 19 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the specific SEQ ID Nos. 1-6 and 9-

12, does not reasonably provide enablement for other nucleotide sequences comprising additional nucleotide flanking sequences and/or allelic variations. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

14. The claimed invention is drawn to DNA related to IgA nephropathy comprising a nucleotide sequence represented by SEQ ID Nos: 1-6 and 9-12 **or** a DNA which hybridizes to said SEQ ID Nos. under stringent conditions. The claims are further drawn to a DNA, and complimentary strand thereof, comprising a nucleotide sequence of 5 to 60 continuous residues that are identical to the DNA of said SEQ ID Nos. 1-6 and 9-12. The claims are further drawn to a method for detecting mRNA of an IgA nephropathy-related gene using, and an IgA nephropathy diagnostic and/or therapeutic agent comprising, any of the aforementioned DNA. The claims are further drawn to a composition comprising any of the aforementioned DNA and a diagnostic and/or pharmaceutical acceptable carrier.

15. The specification teaches the identification of DNA fragments that are more highly expressed in patients with IgA nephropathy as determined by differential mRNA expression between control subjects and patients with IgA nephropathy. The specification further teaches the identification of a putative open reading frame for six of these DNA fragments, SEQ ID Nos:1-6. The specification further teaches an ascribed utility for the claimed DNA fragments as diagnostic markers for IgA nephropathy. The

specification fails to teach allelic variants of the SEQ ID Nos. and/or nucleotide sequences with substitutions, deletions and/or additional flanking sequences.

16. The nature of alleles is that they are variant structures where the structure and function of one does not provide guidance to the structure and function of others. For example, Alberts, *et al.* (page 511) teaches that a family of proteins can "contain a very large number of different proteins and, even for a specific family member, there are often many variants produced either from different genes or from differently processed RNA transcripts from a single gene" and that the isoforms can differ in tissue distribution, cellular location, *etc.*. The identification of SEQ ID Nos. 1-6 and 9-12 does not predict the isolation and characterization of allelic variants of such that have the same structural and diagnostic properties. The nature of alleles is that they are variant structures where the structure and function of one does not provide guidance to the structure and function of others.

17. Furthermore, it is well known in the art that conservative amino acid substitutions may result in altered protein phenotype and/or function. At the time of filing and subsequently thereafter, the state of the art pertaining to conservative modifications embracing amino acid substitutions, deletions, inversions, etc. of a polypeptide is unpredictable with regard to retaining the phenotype of the polypeptide or protein. For example, Ding *et al.* teaches in the abstract of the reference that a single conservative amino acid substitution of alanine with isoleucine in IL-10 converts the protein to a molecule with immunostimulatory activity and that "this single conservative residue alteration significantly affects ligand affinity for receptor."

18. Therefore, it would require undue experimentation to identify allelic variants of the claimed SEQ ID Nos. and to determine the conservative nucleic acid substitutions in the claimed DNAs that would not alter the properties of the DNAs. The amount of experimentation required would include the trial and error determination of substitutions, deletions, inversions, etc. of single and/or multiple nucleic acid residues, and identification of allelic variants, and subsequent hybridization experiments and IgA nephropathy diagnoses for each DNA variant to determine whether or not the diagnostic properties of the DNA are retained. In view of such, the invention is not enabled over the full scope as claimed.

Claim Rejections - 35 USC § 102

19. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

20. Claims 2, 7 and 19 are rejected under 35 U.S.C. 102(b) as being anticipated by Adams, *et al.*, McEver, Kraus, *et al.*, Gerken, *et al.*, Stein, *et al.*, Podgorski, *et al.*, Takeda, *et al.*, Gantt, Linder, *et al.*, and Soares, *et al.*, for SEQ ID Nos: 1, 2, 3, 4, 5, 6, 9, 10, 11 and 12, respectively.

21. The claims have been described in paragraph 15 of the instant office action. The references teach an oligonucleotide stretch of at least 5 residues for each of the claimed

SEQ ID Nos.. The claims read on at least 5 consecutive nucleic acid residues from any oligonucleotide. In view of such, the references clearly anticipate the claimed invention.

Prior art

22. For the record it is noted that SEQ ID Nos: 1-6 and 9-12 are free of the prior art as determined by a standard sequence search comparison against the commercial databases and a literature search.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to David Nikodem whose telephone number is (703) 308-8361. The examiner can normally be reached on M-F, 8:30-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, John LeGuyader can be reached on (703) 308-0447. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 305-3230 for regular communications and (703) 305-3230 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-1123.

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May 22, 2000

JOHN L. LeGUYADER
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600